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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/503,852	02/15/2000	Jonathan L. Tilly	2653/28	5439

23838 7590 03/22/2004

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EXAMINER	
DI NOLA BARON, LILIANA	
ART UNIT	**PAPER NUMBER**
1615	

DATE MAILED: 03/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/503,852	TILLY ET AL.	
	Examiner	Art Unit	
	Liliana Di Nola-Baron	1615	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 26 February 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1.☒ A Notice of Appeal was filed on *26 February 2004*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2.☐ The proposed amendment(s) will not be entered because:

(a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☐ they raise the issue of new matter (see Note below);

(c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____.

3.☒ Applicant's reply has overcome the following rejection(s): 35 U.S.C. 112, first paragraph rejection.

4.☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5.☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6.☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7.☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: *1,5-12,17,18,20-23,32 and 74*.

Claim(s) withdrawn from consideration: _____.

8.☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9.☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10.☐ Other: _____

James M. Spear

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PRIMARY EXAMINER
AU 1615

Continuation of 5. does NOT place the application in condition for allowance because: Applicant's response has not overcome the 35 U.S.C. 103(a) rejection of record.

Applicant's amendment has been entered to simplify the issues for appeal. Applicant's amendment has overcome the 35 U.S.C. 112, first paragraph rejection of claims 1, 2, 4-18, 20-23, 27-36 and 46-80 of the previous Office action. Amended claims 1, 5-12, 17, 18, 20-23, 32 and 74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Perez et al. in view of Spiegel and further in view of Igarashi et al.

Perez et al. indicates that conventional cancer therapies, specifically chemotherapy, kill normal cells and one of the most sensitive noncancerous cell type is the ovarian germ cell, and teaches that apoptosis induced by the chemotherapeutic drug doxorubicin is blocked by sphingosine-1-phosphate (See e.g., p. 1228 and Abstract). Perez et al. teaches that exposure of women to a wide spectrum of agents that damage the ovary generally leads to irreversible sterility (See e.g., p. 1228) and the data from the study provide a strong impetus to manipulate apoptosis caused by chemical drugs in oocytes, in vivo, as a potential means to overcome infertility associated with cancer treatment (See e.g., p. 1231).
Perez et al. does not specify the method and dosage of administration of compositions comprising SPP.

Spiegel provides methods of retarding apoptosis in degenerative diseases, including neurodegenerative diseases and aging, by administration of sphingosine-1-phosphate and derivatives thereof (See e.g., col. 1, lines 9-17). Spiegel teaches that compositions containing SPP may be administered directly to the cells or parenterally to obtain concentrations of 0.1-100 μM, as well as to the epithelial tissues, such as the rectum and the vagina (See e.g., col. 1, line 46 to col. 2, line 42).Igarashi et al. provides methods of inhibiting tumor cell chemoinvasion, comprising administering to a host in need of treatment an inhibitory amount of sphingosine-1-phosphate and teaches that said inhibitory amount can be determined using art-recognized methods, such as dose response curves, or clinical trials, and sphingosine-1-phosphate can be administered orally, parenterally and topically, with suitable doses of sphingosine-1-phosphate depending upon the particular medical application and that the number of doses, daily dosage and course of treatment may vary from individual to individual (See e.g., col. 7, lines 32-65).

Thus, Spiegel and Igarashi et al. provide the teachings that SPP is administered in vivo and disclose a dosage for said administration. Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to apply the teachings of Perez et al. and Spiegel to device methods of protecting the female reproductive system, reviving the ovarian function or ameliorating menopausal syndromes in women, comprising administering SPP compositions, and determining the mode and dosage of administration according to the teachings of Igarashi et al. The expected result would have been successful methods of treatment. Because of the teachings of Spiegel, that sphingosine-1-phosphate is effective in treating aging diseases, and the teachings of Igarashi et al., that sphingosine-1-phosphate inhibits tumor cell chemoinvasion, one of ordinary skill in the art would have a reasonable expectation that the methods claimed in the instant application would be successful. Therefore the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

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